

### REMARKS

In response to the Examiner's Action mailed on February 24, 2004, claims 1 to 10 are amended. The applicants hereby respectfully request that the patent application be reconsidered.

An item-by-item response to Examiner's objections or rejections is provided in the followings:

#### *I. Election/Restrictions*

According to the Examiner, the newly submitted claims 11-20 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: The method of claims 11 do not require that the method be performed by the apparatus of claim. While the method is directed manufacturing the apparatus, the apparatus is not required to be limited to being manufactured by the claimed method. The device may be manufactured from a different process such as first obtaining a block of cured silicone rubber and then etching or carving out material to produce the apparatus. Furthermore, claim 1 does not require that the device be manufactured in a photoresist layer. Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 11-20 are withdrawn from consideration a.s being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP §821.03.

In response to the Examiner's Action, claims 11 to 20 are canceled.

#### *II. Claim Rejections -35 usc§112*

The Examiner rejects Claims 1-6 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 1-6 recite cured silicon rubber, this appears to be improper for silicon is known to be a hard non-metallic element used in alloys and

silicone rubber (the material that applicant appears to be using) is in fact a rubber made from silicone elastomers noted for its retention of flexibility. Claim 5 is indefinite for there is no standard provided for one to determine what is a thickness of a photoresist layer. A photoresist layer can be any thickness desired by the manufacturer. Therefore the photoresist layer of the claim is being considered as any photoresist layer of any thickness. Furthermore, applicant is attempting to provide a structural limitation of the sticks in relationship to a photoresist layer that is not an element of the invention. If applicant intends to claim a specific thickness or thickness range, it should be clearly supported in the specification and claimed in a manner that specifies the thickness. Claim 6 like claim 5 also attempts to limit the structure of the device by describing the elements of the invention in relationship to an unclaimed element (photoresist layer).

In response to the rejections, claims 1-6 are amended and the term "silicon rubber" is amended as "cured silicon rubber" to overcome the rejections.

### *III. Rejection of Claims 35 USC 102:*

The Examiner rejects claims 1 and 5-6 under 35 USC § 102(e) as being anticipated by Birch et. al. US 6,051,1908.

According to the Examiner, Birch et al. disclose an apparatus for the transfer and dispensing small volumes of liquid, especially appropriate in the contexts of biological or chemical analyses and to a method for making the apparatus. First, the material used to make the tool is mixed. In this particular embodiment, the material is a two-component silicone rubber, which is intrinsically non-wettable due to its low surface tension, although any type of intrinsically non-wettable material could be used. In this particular example, the silicone rubber used is SYLGARD 184 from BASF which is mixed with a curing agent in the ration of 10 parts in weight of the curing agent for 100 parts of liquid polymer. Other examples of silicone rubber candidates include SYLGARD 182 from BASF or RTV 630 or 615 from General Electric Co. Next, the mold 30 for making the tool 20 is provided as illustrated in FIGS. 7 and 8A-8D. The mold 30 is a plate 32 with

a plurality of holes 34 which extend through the plate from one surface 36 to the other opposing surface 38 of the plate 32. The diameter of each hole 34 is equal to the desired diameter of pins and the thickness of the plate 32 is equal to the required height of pins to prevent flooding of the rubber tool when the liquid is applied. The placement of the holes 34 in the mold 30 corresponds to the placement of the wells in the mini or micro-well plate. In this particular embodiment, the mold 30 is metallic although the mold 30 could be made out of other materials. Next, one face 38 of the mold 30 is temporarily covered with a removable cover 40 as shown in FIG. 8B. In this particular embodiment, an adhesive tape is used to cover the holes 34 on one surface 38, although other materials to temporarily cover the holes 34 could be used. Once the holes 34 on one face 38 of the plate 32 are blocked, then the material, in this particular example silicone rubber, is poured into the mold 30 as shown in FIG. 8C. The material is then allowed to set for a period of time at room temperature, typically ranging between 15 and 60 hours. In this particular embodiment, the rubber is cured at room temperature, e.g., at about 20 degrees C to 25 degrees C, overnight and is then post-cured at 100 degrees C for 1 hour. After the material is cured, the removable cover 40 is taken off the mold 30 which exposes the drop surface of the rods or pins 18 for the tool 20 as shown in FIG. 8D. The removable cover 40 may also be removed before the rubber is post cured at 100 degrees C for 1 hour.

In response to the rejections, claims 1 to 10 are amended. The amended claims now directed to a refillable stamp array that is totally different, novel and non-obvious over the cited prior art references.

#### ***IV. Rejection of Claims 35 USC 103:***

The Examiner rejects claims 1-6 under 35 USC § 103(a) as being unpatentable over Schurenberg et al. US 6,287,872 in view of Birch et al.

According to the Examiner, Schurenberg et al. disclose an invention that refers to sample support plates for the mass spectrometric analysis of large molecules, preferable bio-molecules, methods for the manufacture of such sample support plates and methods for loading the sample support

plates with samples of biomolecules from solutions together with matrix substance for the ionization of the biomolecules using matrix-assisted laser desorption (MALDI). The droplets are applied in an efficient manner if the multiple pipette is located at a distance of 500 micrometers above the sample support. About 500 nanoliters of sample solution are pipetted from every pipette tip of the multiple pipette onto the sample support as shown schematically in FIG. 1. Usually the amount of sample solution in the pipette tip is sealed off by a gas bubble, therefore there is no more solution present in the channel (microchannel for holding a liquid sample) of the pipette tip afterward and the contact forces to the hydrophobic pipette tip are very minimal. As seen in figure 1 the tapered pipette tips (of at least two different diameters and cross section) labeled as 4 are of the same length and comprise a channel for holding the liquid. Schurenberg et al. does not disclose that the device is composed of silicone rubber. Birch et al. disclose an apparatus for the transfer and dispensing small volumes of liquid, especially appropriate in the contexts of biological or chemical analyses and to a method for making the apparatus. First, the material used to make the tool is mixed. In this particular embodiment, the material is a two component silicone rubber, which is intrinsically non-wettable due to its low surface tension, although any type of intrinsically non-wettable material could be used. In this particular example, the silicone rubber used is SYLGARD 184 from BASF which is mixed with a curing agent in the ration of 10 parts in weight of the curing agent for 100 parts of liquid polymer. Other examples of silicone rubber candidates include SYLGARD 182 from BASF or RTV 630 or 615 from General Electric Co. Next, the mold 30 for making the tool 20 is provided as illustrated in FIGS. 7 and 8A-8D. The mold 30 is a plate 32 with a plurality of holes 34 which extend through the plate from one surface 36 to the other opposing surface 38 of the plate 32. The diameter of each hole 34 is equal to the desired diameter of pins and the thickness of the plate 32 is equal to the required height of pins to prevent flooding of the rubber tool when the liquid is applied. The placement of the holes 34 in the mold 30 corresponds to the placement of the wells in the mini or micro-well plate. In this particular embodiment, the mold 30 is metallic although the mold 30 could be made out of other materials. Next, one face 38 of the mold 30 is temporarily covered with a removable cover 40 as shown in FIG. 8B. In this particular embodiment, an

adhesive tape is used to cover the holes 34 on one surface 38, although other materials to temporarily cover the holes 34 could be used. Once the holes 34 on one face 38 of the plate 32 are blocked, then the material, in this particular example silicone rubber, is poured into the mold 30 as shown in FIG. 8C. The material is then allowed to set for a period of time at room temperature, typically ranging between 15 and 60 hours. In this particular embodiment, the rubber is cured at room temperature, e.g., at about 20 degrees C to 25 degrees C, overnight and is then post-cured at 100 degrees C for 1 hour. After the material is cured, the removable cover 40 is taken off the mold 30 which exposes the drop surface of the rods or pins 18 for the tool 20 as shown in FIG. 8D. The removable cover 40 may also be removed before the rubber is post cured at 100 degrees C for 1 hour.

According to the Examiner, it would have been obvious to one of ordinary skill in the art at the time of the invention to manufacture the device of Schurenberg et al. by allowing the device to be manufactured from silicone cured in a mold as taught by Birch et al. that would allow for a channel to be formed to deposit matrices of biomolecules on a substrate for subsequent analysis.

The Examiner further rejects Claims 7-9 under 35 U.S.C. 103(a) as being unpatentable over Schurenberg et al. in view of Birch et al. as applied to claims 1-6 above, and further in view of Aoki US 6,326,212.

According to the Examiner, the modified teachings of Schurenberg do not disclose the device as having a plurality of micro-stamp tapered channels in fluid communication with one said micro-channel in each of said micro-stamp sticks. Aoki discloses a dispensing apparatuses capable of simultaneously delivering fluid through an array of a plurality of pipettes (sticks). As seen in figure 3 a plurality of spaced rows of concave depressions 42 are provided in bottom plate 39 (substrate). As seen in FIG. 4, each depression 42 has a central hole 43 (FIG. 6) and is aligned at its center or bottom area 44 (tapered) with an elongated needle or pipette 45 (sticks). Each pipette 45 is hollow (micro-channel in stamp sticks) and its interior opens into fluid contact with the interior of each depression 42 via holes 43.

According to the Examiner, it would have been obvious to one of ordinary skill in the art at the time of the invention to recognize that the modified teachings of Schurenberg et al. may be further modified by manufacturing the device to include a tapered micro-channel within the substrate by simply providing a mold of a corresponding shape as such that the tapering allows for sufficient and ease of fluid supply to each stick.

The Examiner further rejects claim 10 is rejected under 35 U.S.C. 103(a) as being unpatentable over Schurenberg et al. in view of Birch et al. and Aoki as applied to claims 7-9 above, and further in view of Sunberg et al. US 6,451,188.

According to the Examiner, the modified teachings of Schurenberg do not teach a refilling means for refilling each of said plurality of micro-stamp tapered channels wherein said refilling means further comprising a refilling reservoir and a plurality of refilling micro-channels for refilling each of said plurality of micro-stamp tapered channels from said refilling reservoir. Sunberg et al. disclose a system and apparatus in which fluid introduction is facilitated through the use of a port which extends entirely through a microfluidic substrate. Capillary forces can be used to retain the fluid within the port, and a series of samples or other fluids may be introduced through a single port by sequentially blowing the fluid out through the substrate and replacing the removed fluid with an alternate fluid, or by displacing the fluid in part with additional fluid. As seen in figure 3 the structure of the microfluid substrate which allows access to the microfluidic channels introducing fluids and other materials. The device comprises a refilling means that is comprised of multiple refilling reservoirs and refilling micro channels connected with and supplying fluid to the ports 34. Sunberg further discloses micro-fluidic analytical systems have a number of advantages over conventional chemical or physical laboratory techniques. For example, microfluidic systems are particularly well adapted for analyzing small sample sizes, typically making use of samples on the order of nano-liters and even pico-liters. The substrates may be produced at relatively low cost, and the channels can be arranged to perform numerous specific analytical

operations, including mixing, dispensing, valving, reactions, detections, electrophoresis, and the like. The analytical capabilities of microfluidic systems are generally enhanced by increasing the number and complexity of network channels, reaction chambers, and the like.

According to the Examiner, it would have been obvious to one of ordinary skill in the art at the time of the invention to modify the modified teachings of Schurenberg et al. manufacturing the device to include the fluid supply system of Sunberg in order to provide a constant supply of fluid to the sticks and to dispense small samples on the order of nano-liters and pico-liters.

In response to the rejections, claims 1-10 are amended. The amended claim 1 is directed to a micro-stamp array that has specific refilling chip and having tapered guide tubes as fully supported by the specification and are totally new and not obvious over the cited prior art references. The amended claims 1 to 10 would be non-obvious and patentable over Schurenberg, Sunberg, and Aoki.

With the amended claims and the reasons provided above, the applicant hereby respectfully urges that Examiner's rejections under 35 USC § 112, 35 USC § 102 and 35 USC § 103 of the claims be withdrawn and the present application be allowed.

Respectfully submitted  
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By



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